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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/758,962	01/09/2001	Simon Santa-Cruz	00801.0192.NPUS00	9671

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EXAMINER	
QIAN, CELINE X	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 07/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/758,962	SANTA-CRUZ ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-30,38 and 53-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *4 and 38* is/are allowed.

6)☒ Claim(s) *1-3,5,7-30 and 53-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 January 2001* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5, 7-30, 38, 53-56 are pending in the application.

This Office Action is in response to the Amendment filed on 5/9/05.

Response to Amendment

The rejection of claims 3 and 4 under 35 U.S.C. 112 1st paragraph has been withdrawn in light of Applicant's amendment of the claims.

The rejection of claims 9-11 under 35 U.S.C. 102 (b) is maintained for reasons set forth of the record mailed on and further discussed below.

The rejection of claims 1-3, 5, 7-8, 12-30 and 53 under 35 U.S.C.103 (a) for reasons set forth of the record mailed on and further discussed below.

The rejection of claims 54-56 under 35 U.S.C.103 (a) is withdrawn in view of the 102(b) rejection as set forth below.

Claims 55 and 56 are rejected under 35 U.S.C.112 2nd paragraph for reasons set forth below.

Response to Arguments

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Ivanov et al.

In response to this rejection, Applicants argue that Ivanov does not include all limitation of the claims. Specifically, Applicants assert that the vector, pHβΔNPTCP taught by Ivanov does not contain an IRES capable of directing the expression of an internal ORF in a heterologous plant viral vector. Applicants further assert that the constructs on page 39 of this reference are not heterolgous plant viral vectors that are equivalent to the recombinant plant viral vectors of the instant claims. Applicants alleges that the examiner uses the term "vector" too generically, wherein the claimed plant viral vectors are optionally used to replicate in plants and to infect plants in vivo as opposed to the non-infectious plasmids taught by Ivanov. Applicants assert that the present invention comprises plant viral vectors comprising modified virus capable of expressing a desired protein or trait in a host, which is not disclosed in Ivanov. Moreover, Applicants assert that the coat proteins in the Ivanov plasmids are from crTMV as are the IRES sequence. Applicants thus conclude that claims are not anticipated by Ivanov et al.

The above arguments are fully considered but deemed unpersuasive. Although the Examiner mis-quote the reference on page 33, the teaching of Ivanov et al. still anticipates the claimed invention. The Examiner would like to point out that it is the vector pHβΔNPTIREScpCP, rather than pHβΔNPTCP, comprises the 148nt IRES isolated from crTMV (see page 33, 2nd col., 4th paragraph, lines 14-17, and Figure 4D). In response to Applicant's argument with regard to the differences between the vectors, Applicants are reminded that the claims are drawn to an IRES capable of directing the expression of an internal ORF in a heterologous plant viral-based vector, rather than a vector construct itself. Claims 10 and 11 are further drawn to an IREScp and an IREScp from crTMV. Ivanov discloses an IREScp isolated from crTMV. Absent evidence from the contrary, the ability of the claimed IRES to direct

expression in a heterolgous plant viral-based vector does not impart a structural difference from the IRES disclosed by Ivanov. As such, the interpretation of the "vector" is irrelevant to the novelty of the claimed invention because it is not a limitation of the instant claims. Similarly, whether the coat protein in the construct taught by Ivanov is heterologous to the IRES also is irrelevant because a heterolgous construct is not part of the claim limitation. Therefore, for reasons set forth in the previous office action and above, the claimed invention is anticipated by Ivanov. This rejection is thus maintained.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3, 5, 7-8, 12-30 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Santa Cruz et al., in view of Ivanov et al.

In response to this rejection, Applicants argue that there is no motivation to combine the references. Applicants assert that the proposed modification of Santa Cruz by addition of IRES sequences would render Santa Cruz's constructs unsatisfactory for their intended purposes. Applicants assert that the production of PVX.GFP-CP virions requires both the fusion protein and free coat protein, wherein lack of the fusion protein will not produce the desired virion assembly and spread throughout the plant. Applicants indicate that Santa Cruz specifically discusses the method to decrease the 2A cleavage of the fusion protein so that more fusion protein remains, such that increase the production of CP would be counter productive to the goal of Santa Cruz. As such, Applicants assert that there is no motivation to combine the references. Moreover, Applicants argue that there is no motivation to read Ivanov into Santa Cruz because

the construct system used in these references are different. Applicants assert that Ivanov desires separate protein production, whereas Santa Cruz does not desire totally separate protein production. Furthermore, Applicants argue that Ivanov teach that IRES in general are divergent and that core functional areas of IREScp were not known by Ivanov at the time. Applicants assert that the uncertainty to the parameters of the TMV IREScp and the different types IRES sequence support Applicant's position that there is no motivation to combine the reference. Moreover, Applicants argue that there is no expectation of success in combine the two references because the references uses different vector system (*in vitro* vs. *in vivo*). Applicants argue that there is quite a degree of unpredictability which would arise in combine the references because an operable system *in vitro* would not necessarily be operable *in vivo*. Applicants assert that many potential problem can arise in construction/design of *in vivo* constructs. Applicants further assert that two methods differ greatly in their translation strategies, wherein one uses IRES have multiple translation events, whereas the other uses a single translation with cleavage of a fusion protein. Applicants argue that due to the disparity of the systems, there is no reasonable expectation that the addition of IRES from Ivanov to Santa Cruz's structure would give better results. Applicants thus conclude that the rejection is improper.

The above arguments have been fully considered but deemed unpersuasive. The reasons for the obviousness of the claimed invention in view of the cited references were discussed in detail in previous office actions. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references

themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the motivation to combine is clearly indicated in the previous office action, which is increasing free CP production, which is required for packaging and cell-to-cell movement of the PVX based vector for infection (see page 6287, 2nd col., 1st paragraph and page 6288, 1st col., 1st paragraph). Applicant's interpretation of the text on page 6287 is erroneous because assembly of the virion does not require the presence of a fusion protein that comprises GFP and CP, although it is rather obvious that packaging of the fusion protein requires both the fusion protein and free CP. In other words, the packaging of other protein does not require such a fusion protein. The 3rd paragraph on page 6287 merely discusses the 2A mediated processing of post-translational cleavage of a synthetic polyprotein is not as efficient as its function in FMDV 2A/2B junction, thus one would expect the fusion of GFP-CP through this peptide would result in a mixture of fusion and free protein. Such teaching is clearly very different from Applicant's conclusion that it teaches methods of decreasing 2A cleavage so that more fusion proteins would remain. Applicants are invited to provide evidence if such teaching is provided by this reference. Applicants have not provided reasons for why the production of free CP would be counter productive to the purpose of Santa Cruz. After all, Santa Cruz teaches vector systems for producing proteins in plant (see page 6290, 1st paragraph, 1st paragraph, lines 1-5), whereas the GFP-CP is just an example of a protein of interest. Producing proteins such as GFP, or other proteins, would require free CP, rather than the fusion GFP-CP for virion package and expression in plants.

In response to Applicant's argument with regard to different systems in the references, Applicants are reminded that the claims are drawn to a viral vector regardless of its use *in vivo* or *in vitro*. As such, whether the constructs in the references are *in vitro* or *in vivo*, and the purpose of making said constructs are irrelevant. Applicants are again reminded that although Ivanov does not disclose the core functional area of the IRES, this reference does teach the 148nt sequence does have IRES activity. Besides, the claims do not have the limitation of defined core functional areas of the IRES. Moreover, Applicants clearly misconstrue the teaching of Ivanov stating IREScp is "markedly distinct" from IRESes of other sources, which is directed to structural difference, rather than its ability to initiate translation (in other words, to function as IRES). As such, there is reasonable expectation of success of this IRES to function in a viral vector. Moreover, Applicants' interpretation of "reasonable expectation of success" is erroneous because it refers reasonable expectation of success in making the claimed invention. The statue does not require reasonable expectation of success in improving over the prior art. As such, based on the teaching of Santa Cruz and Ivanov, there is reasonable expectation of success in making a plant viral construct, and adding an IREScp between two ORF for proper expression of both ORF. Again, since the claims do not have any limitation of *in vivo* or *in vitro* use, the predictability of whether one would function in another system is irrelevant. Furthermore, whether there is a disparity between the systems used in two references is also irrelevant. The claimed invention is obvious in view of the cited art because the art teaches every element of the claimed invention and provides sufficient motivation and reasonable expectation of success to make the claimed invention. Therefore, for reasons discussed in the previous office action and above, this rejection is maintained.

Claims 54-56 are not included in this rejection in view of the new grounds of rejection discussed below.

New Grounds of Rejection

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 54-56 are rejected under 35 U.S.C. 102(b) as being anticipated by Skulachev et al. (see IDS, Virology, 1999, Vol. 263, pages 139-154).

The claims are drawn to a recombinant or isolated polynucleotide comprising: an IRES nucleotide sequence, an ORF encoding a peptide of interest, and an ORF encoding a viral protein, wherein the IRES is located in between the peptide of interest and the viral protein, and wherein the IRES is heterologous to the viral protein. The claims are further drawn to said polynucleotide sequence wherein the IRES or viral protein nucleotide sequence comprises a tobamovirus nucleotide sequence, and/or said tobamovirus comprises crTMV.

Skulachev et al. discloses constructs (which are recombinant polynucleotide) that comprises an IRES from MP of the TMV U1 located in between CP (a viral protein from crTMV) and GUS gene (see for example, page 143, Figure 3B or D). Said IRES is heterologous to the CP protein from crTMV. Therefore, Skulachev et al. disclose the instantly claimed inventions.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 55 and 56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 55, the recitation of "one or more of the IRES nucleotide sequence or the viral ORF" renders the claim indefinite because it is unclear how many IRES or viral ORF the polynucleotide comprises. Claim 54, the parent claim which 55 depends on, only recites one IRES and one viral ORF, whereas claim 55 recites one or more IRES and viral ORF. As such, the metes and bounds of the claim cannot be established. Claim 56 is indefinite because it depends on claim 55.

Claims 4 and 38 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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